REMARKS

Claims 33-34, 38-40, 87, 89, 92, 101, 103-107 and 109-122 are currently pending.

Claim 33 has been amended to recite, *inter alia*, a method of treating a hepatitis C virus infection in a host comprising (a) administering a 2'-branched nucleoside, (b) identifying viral resistance to the 2'-branched nucleoside, and (c) administering one or more additional drugs that induce a mutation in the virus at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region. Support for this amendment is found, for example, at page 31, line 28 to page 32, line 9; and page 49, lines 1-10. Claim 33 has also been amended to delete "optionally in a pharmaceutically acceptable carrier or diluent."

Claim 107 has been amended to depend only from claim 33.

New claim 109 recites the method of 33 wherein the 2'-branched nucleoside is in a pharmaceutically acceptable carrier or diluent, and is supported, for example, by original claim 1.

New claim 110 recites the method of claim 33 wherein the drug of step (c) is interferon. Support for claim 110 is found, for example, at page 32, lines 8-9 and page 80, lines 14-20 of the specification.

New claim 111 recites the method of claim 33 wherein identifying viral resistance in step (b) comprises assaying the blood of the host to test for seroconversion from wildtype to mutant virus. Support for claim 111 is found, for example, at page 32, lines 6-7 of the specification.

New claims 112 and 113 recite the method of claim 33 wherein identifying viral resistance in step (b) comprises phenotypic analysis of viral plaque growth. Support for claims 112 and 113 is found, for example, at pages 80-81 of the specification.

New claims 114 and 115 recite the method of claim 33 wherein identifying viral resistance in step (b) comprises determination of the replication fitness of the virus. Support for claims 114 and 115 is found, for example, at pages 80-81 of the specification.

New claim 116 recites the method of claim 33 wherein identifying viral resistance in step (b) comprises detecting the presence of cytidine at nucleotide 8443 of the RNA

polymerase region of the hepatitis C virus. Support for this claim is found, for example, at page 80, lines 25-28.

New claim 117 recites, *inter alia*, the method of claim 33, wherein identifying viral resistance in step (b) comprises detecting hybridization of an oligonucleotide probe with a sample from the infected host. Support for this claim is found, for example, at page 19, line 29 to page 20, line 5 of the specification.

New claims 118 and 119 recite methods of treating a hepatitis C virus infection in a host infected with a hepatitis C virus that contains a mutation in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region. This claim is supported, for example, by page 90, lines 15-20.

New claim 120 recites the method of treatment of amended claim 33, wherein the genus of compounds is of formula IV, and wherein Base is a pyrimidine. Support for this claim is found, for example, at pages 13, 31-32 and 49 of the specification.

New claim 121 recites the method of claim 33, wherein the compound of the formula of claim 33 is administered. Support for this claim is found, for example, at pages 11-12 of the specification.

New claim 122 recites the method of claim 120, wherein the compound of formula IV is administered. Support for this claim is found, for example, at page 13 of the specification.

No new matter has been added by the amendments.

Applicants point out that the amended claims are within group IV of the Restriction Requirement dated March 7, 2007.

I. Claims Rejections under 35 U.S.C. § 102.

The Examiner has maintained the rejection of claims 33-34, 92, 104 and 107 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 7,105,499 to Carroll *et al.* ("Carroll"). Specifically, the Examiner alleges that the instant claims are anticipated because Carroll discloses 2'-C-methyl cytidine in combination with other agents selected from a list of compounds. (Office Action, page 4). Applicants respectfully disagree.

The Examiner argues that the term "optionally" before the phrase "in combination and/or alternation with one or more drugs that directly or indirectly induce a mutation in a hepatitis C virus at a location other than a mutation of a nucleotide that results in a change

from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region" in claim 33 should be read such that the mutation language is not a claim limitation. (Office Action, page 5). While Applicants disagree with the Examiner's interpretation of claim 33, the point is moot because amended claim 33 no longer recites the term "optionally."

The Examiner further alleges that because (1) Carroll teaches 2'-C-methyl cytidine for the treatment of a hepatitis C virus infection, (2) the compounds of Carroll, including 2'-C-methyl cytidine, may be combined with a list of second agents including interferon, and (3) interferon induces a mutation in the hepatitis C virus at a location other than serine in the highly conserved consensus sequence of domain B of the RNA polymerase region, the instant claims are inherently anticipated by Carroll. (Office Action, pages 5-6). Applicants respectfully disagree.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131, *quoting Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (emphasis provided). Amended claim 33 recites, *inter alia*, a method of treating a hepatitis C virus infection in a host comprising (a) administering a 2'-branched nucleoside, (b) identifying viral resistance to the 2'-branched nucleoside, and (c) administering one or more additional drugs that induce a mutation in the virus at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region. Because Carroll does not disclose any of the elements of steps (b) or (c) of claim 33, the instant claims are not anticipated by Carroll. *See Id.* at 631. Claims 34, 92, 104 and 107 each depend from claim 33. Therefore, Applicants respectfully request that the rejection of claims 33-34, 92, 104 and 107 under 35 U.S.C. § 102(e) be withdrawn.

II. Claims Rejections Under 35 U.S.C. § 103.

The Examiner has maintained the rejection of claims 39-40, 89, 101, 103, 105 and 106 under 35 U.S.C. § 103(a) as allegedly obvious over Carroll in view of Sinko *et al.* (Office Action, page 7). Specifically, the Examiner alleges that because Carroll teaches 2'-branched ribonucleosides in combination with second antiviral agents, and Sinko teaches that the use of a valine ester increases the bioavailability of acyclovir, the instant claims are obvious. (*Id.*). Applicants respectfully disagree.

As discussed above, claim 33 has been amended to recite, *inter alia*, a method of treating a hepatitis C virus infection in a host comprising (a) administering a 2'-branched nucleoside, (b) identifying viral resistance to the 2'-branched nucleoside, and (c) administering one or more additional drugs that induce a mutation in the virus at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region. Rejected claims 39-40, 89, 101, 103, 105 and 106 depend from claim 33.

Neither Carroll nor Sinko teaches or suggests the method of amended claim 33. While Carroll discloses 2'-branched ribonucleosides used in combination with additional antiviral agents, Carroll does not disclose, teach or suggest viral resistance or methods of treating resistant strains of hepatitis C virus.

Sinko does not cure the defects of Carroll because Sinko merely teaches that the valine ester of acyclovir has improved oral bioavailability. Because Sinko is silent as to the genus of compounds of claim 33, viral resistance, and methods of treating resistant strains of hepatitis C virus, one of ordinary skill in the art would have no reason to combine the teachings of Carroll and Sinko to arrive at amended claim 33. *See KSR International Co. v. Teleflex Inc.*, 127 L.Ed.2d 705, 82 U.S.P.Q.2d 1385, 1395 (2007) (Examiner must "identify a reason that would have prompted a person of ordinary skill...to combine the elements in the way the claimed new invention does."); *see also Takeda Chemical Ind., Ltd. v. Alphapharm Pty., Ltd.*, 429 F.3d 1350, 1356 (Fed. Cir. 2007) (The current law of obviousness in cases concerning structurally similar compounds "requires a showing of 'adequate support in the prior art' for the change in structure."). For at least these reasons, amended claim 33 is not obvious over Carroll in view of Sinko. Because claims 39-40, 89, 101, 103, 105 and 106 depend from claim 33, they are also not obvious over Carroll in view of Sinko. Therefore, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 103.

CONCLUSION

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The fee for a one month extension of time wil be paid via EFS Web. Please charge any additional required fees, or any credits, to Jones Day deposit account no. 50-3013 (referencing 417451-999064).

If the Examiner believes it would be useful to advance prosecution, the Examiner is invited to telephone the undersigned at (858) 314-1200.

Respectfully submitted,

Date: September 26, 2008

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